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Further Studies of the Cycloplegic Value of Homatropine *Plus* Cocaine Discs as Atropine, Duboisine and Hyoscine Substitutes.

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[*Read before the Section of Ophthalmology, Pan-American Medical Congress, Washington, D. C., 1893.*]

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FURTHER STUDIES OF THE CYCLOPLEGIC VALUE OF HOMATROPINE *PLUS* COCAINE DISCS AS ATROPINE, DUBOISINE AND HYOSCINE SUBSTITUTES.

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NEARLY three years ago, in an article contributed to the *American Journal* of *Ophthalmology*, I gave the results of some experiments I had made with mixtures of Homatropine *plus* Cocaine, and with solutions of Atropia and Duboisine for the purpose of comparing their relative merits as Cycloplegics. The conclusions I then arrived at were these:

1. In the shape of watery solutions probably less than ten per cent. of the dissolved alkaloid becomes absorbed in such a way as to affect the eye, the remaining ninety per cent. or more being carried off into the nasal duct or flowing over the cheek with the tears.

2. Mixtures prepared with Vaseline, Cosmoline, Sanitas Jelly, Lanoline and similar menstrua or, as in Lang and Barrett's* experiments, Castor Oil, are much longer retained in the conjunctival sac. The drugs thus longer kept in contact with the ocular and palpebral surfaces undergo, as Green suggests, a much more extensive absorption and produce a still more pronounced effect.

3. They are absorbed by the blood vessels and other absorbents of the cornea and conjunctiva and not by those of the nose and throat. But such oily and greasy mixtures have this serious drawback: they leave a thin film upon the corneal surface which interferes with the examination of the eye especially when one wishes to determine its refractive condition.

*LANG AND BARRETT: The action of Myotics and Mydriatics. *Oph. Hos. Reports*, vol. xi., pp. 130 and 219.

4. The form of gelatine lamellæ or discs appears to be the most useful one in which to apply agents to the eye for the purpose of securing their fullest mydriatic and cycloplegic action. These undergo a slow, regular and complete absorption when put into the conjunctival sac.

5. The addition of Cocaine to almost all the alkaloids used in ophthalmic practice undoubtedly increases their peculiar effects. (See also the reports of Maklakoff* and the experiments of Lang and Barrett aforementioned.)

6. From the foregoing results and after much experimentation on the subject, I concluded that the most decided cycloplegic effects of Homatropine are obtainable from its employment in the gelatine disc form, associated with Cocaine.

In their most convenient and stable shape these discs cannot be made to hold more than gr. 1/25 of these alkaloids; hence I was necessarily restricted to the use of gr. 1/50 each of Merck's Homatropine and Cocaine.

Since the publication of my original paper I have not lost sight of the purpose I then had in view, viz: the attempt to find some cycloplegic less objectionable than Atropine for the measuring of refractive errors. I happen to be a firm believer in the doctrine that it is necessary to know the absolute refractive condition before one can intelligently prescribe glasses, and I further believe that it is requisite to paralyze the accommodation as the best means of obtaining that information in the majority of patients under, and is some instances over, forty years of age.

For the past year I have been engaged in this line with the gelatine discs aforesaid, with discs containing gr. 1/25 of Homatropine alone, and with various solutions in water of Tropa-cocaine, Homatropine plus Cocaine, Duboisine Sulphate, Atropine Sulphate, Hyoscin Hydrobromate and Hyoscyamin Sulphate.

Without troubling you with details I may say, briefly, that for the determination of the refractive condition and with the idea of making the conditions of the comparative test as constant as possible I chose those patients in whom I could employ a number of agents at proper intervals and whose refractive state would be most likely to afford reliable tests. These were put under the influence of the particular cycloplegic and their refractive state determined by skiascopy. Every case was carefully worked out by my assistant, Dr. T. A. Woodruff, who is an expert skiascopist.

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* *Sajou's Annual*. vol. iv., p. 157, 1889.

Sometimes one agent was used first, sometimes another, but in every instance the effect of the previous cycloplegic was allowed to pass off before the second was employed. Using all possible care to avoid sources of error, the refraction of thirty-four selected eyes, furnishing sixty-eight principle meridia was thus determined. The results I have here drawn up in chart form:

	Atropia.	Hyoscin.	H. & C. Discs		Atropia.	Hyoscin.	H. & C. Dics.
1.	+3.	+3.25	+3.	35.	+5.	+4.50	+5.
2.	+1.75	+1.75	+1.75	36.	+6.50	+6.50	+6.50
3.	+2.75	+2.50	+2.50	37.	+5.	+5.	+5.
4.	+1.50	+1.50	+1.50	38.	+6.	+5.50	+6.
5.	+0.75	+0.50	+0.50	39.	+5.		+4.50
6.	+4.	+4.25	+4.	40.	+8.		+8.
7.	+2.25	+2.25	+2.	41.	+4.50		+4.
8.	+3.25	+3.50	+3.25	42.	+6.		+6.
9.	+1.25	+1.75	+1.55	43.	+8.		+8.
10.	+2.50	+2.75	+ +2.75	44.	+9.		+9.
11.	+1.50	+1.50	+1.50	45.	+10.		+9.50
12.	+2.75	+3.	+2.75	46.	+11.		+10.50
13.	+2.75		+2.50	47.	+1.25		+1.25
14.	+2.75		+2.50	48.	+1.50		+1.50
15.	+2.75		+2.50	49.	+2.		+1.75
16.	+2.75		+3.	50.	+2.25		+2.25
17.	+5.	+5.50	+5.	51.	+2.25		+2.25
18.	+5.	+6.	+5.50	52.	+2.25		+2.25
19.	+6.25	+5.50	+6.	53.	+7.		+7.
20.	+7.	+7.	+6.50	54.	+11.		+11.
21.	+1.75		+1.25	55.	+6.50		+6.50
22.	+1.25		+1.25	56.	+10.		+9.50
23.	+1.50		+1.25	57.	+3.25		+3.
24.	+1.75		+1.50	58.	+3.		+3.
25.	+3.75	+3.75	+3.75	59.	+3.25		+3.25
26.	+5.50	+5.	+5.50	60.	+3.		+3.
27.	+2.50	+2.75	+2.50	61.	+1.50		+1.50
28.	+3.50	+3.25	+3.50	62.	+3.50		+3.50
29.	+6.50	+7.	+6.25	63.	+ 3.75		+3.75
30.	+6.50	+7.	+6.50	64.	+2.		+2.
31.	+2.25		+2.	65.	—1.	—1.	—1.
32.	+2.		+1.50	66.	+1.25	+1.25	+0.50
33.	+1.50		+1.50	67.	+4.50	+4.	+4.50
34.	+1.50		+1.50	68.	+5.50	+5.50	+3.75

In these observations (166 in all), two drops of a one per cent. solution of Atropia Sulphate were dropped into each eye three times daily after meals for two days, and the examination made in from one to three hours after the last instillation. Of the Hyoscin and Hyoscyamin two drops of

a four grain solution were instilled into each eye three times, at intervals of twenty minutes, and the examination made in from one to two hours after the last dose.

The discs were employed as hereafter described. Every precaution was taken to prevent poisoning by the Hyoscin and Hyoscyamin.

Atropia, Hyoscin and the discs were used for the examination of the same meridia in thirty instances. In sixteen of these the refraction was exactly the same, or the highest differed from the lowest not more than 0.25 D. In ten instances the difference was 0.50 D. In only two instances out of the thirty was there a greater difference than 0.50 D., a case to be afterwards referred to.

In these thirty cases Atropia showed the highest refraction, or was one of the highest in nineteen instances; Hyoscin in twenty-two instances and Homatropine and Cocaine discs in fifteen instances.

Coming now to the tests of Atropia and Homatropine *plus* Cocaine discs we found that they were the same or did not vary more than 0.25 in fifty-eight out of sixty-eight meridia. In the remaining ten the result varied +0.50 in eight cases, and in two instances there was a radical difference, to be again referred to. Speaking generally Atropia showed a higher refractive condition than the discs in twenty-one out of sixty-eight cases, while the discs showed an increased refraction over Atropia in four instances. In a single instance of mixed astigmatism, before referred to, did the refraction of two principal meridia amount to more than +0.50, viz: 0.75 D. and 1.75 D. greater in the case of Atropia than that shown by the discs. In this case the discs were first used. That this may happen in a second trial of any cycloplegic (in relieving a spasm of the accommodation) is well known. I have recently had a case, which well illustrates this fact, where a second trial with Atropia revealed a much greater difference.

A boy, aged 16, with V. = $\frac{6}{9}$—and marked astigmatism in each eye, was atropinized in the usual way with a one per cent. solution and the skiascopy result was:

+2.75	+3.50
+2.50	+3.25.

A week later he was found to have, with full correction, 9/6 nearly in either eye. My suspicion being aroused by this early acceptance of his glasses, I again atropinzed his eyes and the result was:

+4.	+4.75
+4.50	+5.25

i. e. an advance of between 1.25 D. and 2. D. in the four meridia Ten days

afterwards he obtained vision 6/6— in either eye. A month afterwards his vision in each eye was 6/6+ with all symptoms relieved.

As a result of these and other experiments I have reached the following conclusions, some of which are modifications of the propositions contained in my first article:

1. If two gelatine discs containing gr. 1/50 each of Homatropine *plus* Cocaine be placed in the conjunctival sac at an interval of twenty minutes, *the eye being all the while kept closed*, the ciliary muscle will in most instances be found to be fully paralyzed in from seventy to one hundred minutes after the introduction of the first disc.

2. In persons under twenty-five years of age, or whenever ciliary spasm is suspected, the best results are obtained by the use *in another twenty minutes of a third disc or one containing gr. 1/25 of Homatropine alone*, the examination in that case being best made between ninety and one hundred and twenty minutes after using the first disc. The first two discs containing Cocaine are sufficient to furnish the chief advantage which in my opinion resides in that alkaloid, viz: of increasing the absorbing powers of the cornea for agents combined with it, while the increased dose of Homatropine produces a more thorough relaxation of the ciliary muscle.

An eserine disc (gr. 1/1000) inserted the following morning will enable the patient to do near work within an hour or two.

3. The discs should be inserted on the tip of a damp camel's-hair brush and should always be applied to the ocular conjunctiva at its inferior and outer surface, the patient looking up and in, while the lower lid is drawn down. Any adherent or sticky gelatine may be easily wiped off the palpebral edges with a damp cloth or a piece of wet absorbent cotton, before making the examination.

In my preference for these discs over any solution of Atropia I wish to state that I do so only on the grounds of the quicker and more evanescent cycloplegic action of the former.

I always use Atropia whenever I possibly can, and particularly if, in my judgment, the patient would be benefited by ciliary rest, as many of our cases are. But for the business man, the clerk, the book-keeper, the doctor, the school teacher, *et hoc genus omne* ten days of ciliary or any other kind of rest is usually impossible. It is with them either an examination for glasses of the optician-and-jewelry-store order or a transient cycloplegia.

In the list of dangerous cycloplegics I would place Duboisin, Hyoscin and Hyoscyamin. They are all, especially the last two, much prompter

and more fiercely active cycloplegics than Atropia or these discs. If Hyoscin and Hyoscyamin are used in solution and in doses strong enough to insure ciliary paresis—i. e. in doses somewhat less than Atropia and Duboisin they are certain to produce toxic symptoms more or less pronounced in about one quarter of the cases. If used at all they should be instilled in the oculist's office, and in my experiments I found this to be the only safe plan to pursue.

If this be done the refractive condition can be readily determined in one day, the ciliary paresis passing off in from seventy-two to ninety-six hours. Upon their cycloplegic action single discs of Eserine have little or no permanent effect.

Tropa-cocaine has, so far as my experiments went, no cycloplegic advantages over Cocaine while its mydriatic action seemed to me to be less than that of Cocaine.

I take pleasure in stating that the Discs used in my experiments were made for me by Messrs. JOHN WYETH & BROTHER, the well-known Manufacturing Chemists of Philadelphia.

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